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- (71) Applicant (*for all designated States except US*): ELI LILLY AND COMPANY [US/US]; Lilly Corporate Center, Indianapolis, IN 46285 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): YAKUBU-MADUS, Fatima, Emitsel [NG/US]; 9303 Timberline Drive, Indianapolis, IN 46256 (US). STRAMM, Lawrence, E. [US/US]; 9143 Hadway Drive, Indianapolis, IN 46256 (US). JOHNSON, William, T. [US/US]; 1367 Maynard Drive, Indianapolis, IN 46227 (US). VIGNATI, Louis [US/US]; 5617 North Meridian Street, Indianapolis, IN 46208 (US).
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12 July 2001
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(54) Title: SYNERGETIC USE OF THIAZOLIDINEDIONES WITH GLUCAGON-LIKE PEPTIDE-1 AND AGONISTS THEREOF TO TREAT NON-INSULIN DEPENDANT DIABETES

(57) Abstract: Thiazolidinedione (TZD) and its pharmacologically active derivatives can be used, in combination with agonists of glucagon-like peptide-1 (GLP-1), to treat non-insulin dependent diabetes mellitus, optionally with other therapies, by improving glycemic control while minimizing side effects, such as heart hypertrophy and elevated fed-state plasma glucose, which are associated with both TZD and GLP-1 monotherapies. Thus, the co-administration of TZD and GLP-1 helps regulate glucose homeostasis in Type II diabetic patients.

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INTERNATIONAL SEARCH REPORT

Intern. Application No.

PCT/US 00/15548

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/22 A61K38/26 A61P3/08 //(A61K38/22,31:425)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, MEDLINE, BIOSIS, PAJ, WPI Data, CANCERLIT, AIDSLINE, LIFESCIENCES, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>REASNER, C. A., II: "Promising new approaches" DIABETES, OBES. METAB. (1999), 1(SUPPL. 1), S41-S48, XP000971954 page S41, paragraph 1 -page S42 page S43, column 1, paragraph 3 -column 2, paragraph 3 page S44, column 1, paragraph 2 -page S45, column 2, paragraph 1</p> <p style="text-align: center;">---</p>	1-14, 19-21
Y	<p>WO 98 57636 A (SMITH STEPHEN ALISTAIR ;SMITHKLINE BEECHAM PLC (GB)) 23 December 1998 (1998-12-23) page 1, line 9 - line 37 page 3, line 28 - line 31 page 4, line 4 - line 6 page 5, line 6 - line 21</p> <p style="text-align: center;">---</p> <p style="text-align: center;">-/--</p>	1-14, 19-21

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

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Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Noë, V

INTERNATIONAL SEARCH REPORT

Intern Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 631 224 A (EFENDIC SUAD ET AL) 20 May 1997 (1997-05-20) cited in the application	15-18,22
Y	abstract column 2, line 65 -column 3, line 40 column 4, line 47 - line 63 column 5, line 16 - line 20 examples 1,2 ---	1-14, 19-21
X	EP 0 733 644 A (LILLY CO ELI) 25 September 1996 (1996-09-25) abstract page 6, line 3 - line 20 page 7, line 55 -page 8, line 4 page 8, line 16 - line 22 page 8, line 36 - line 41 ---	15-18,22
A	WO 99 03478 A (BUCKINGHAM ROBIN EDWIN ;SMITH STEPHEN ALISTAIR (GB); SMITHKLINE BE) 28 January 1999 (1999-01-28) the whole document ---	
P,X	WO 00 00195 A (ODAKA HIROYUKI ;YAMANE MASAHIRO (JP); TAKEDA CHEMICAL INDUSTRIES L) 6 January 2000 (2000-01-06) abstract page 3, line 16 - line 24 page 20, line 11 - line 15 page 21, line 1 - line 13 page 25, line 29 -page 26, line 27 page 27, line 27 -page 28, line 15 page 28, line 31 -page 29, line 13 page 30, line 2 - line 5 -----	1,2, 4-12,14, 19-21

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1 and 4 relate to compounds defined by reference to a desirable characteristic or property, namely incretin hormone is any hormone that is released after meals and that potentiates insulin secretion (claim 1) and glp-1 analog is any product that is structurally or functionally related to glp-1 (claim 4).

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to compounds mentioned in the description on page 9, line 20-26, page 13, line 1-22 and in claims 2 and 3.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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